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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/849,525	08/29/1997	GHITA LANZENDORFER	435-WCG	3976

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NORRIS, MCLAUGHLIN & MARCUS, P.A.
220 EAST 42ND STREET
30TH FLOOR
NEW YORK, NY 10017

EXAMINER
SHARAREH, SHAHNAM J

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 05/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/849,525	LANZENDORFER ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 27 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on January 31, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/849,525 is acceptable and a CPA has been established. An action on the CPA follows.

Status of the claims

2. Preliminary Amendment filed on January 31, 2001has been entered. Claims 19-33 are now pending.

Response to Arguments

3. Applicant's arguments with respect to claims 8, 11-16 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 19-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating immunosuppression comprising administering at least one flavonoid, does not reasonably provide enablement for methods of preventing immunosuppression of skin cells induced by UVB radiation. Accordingly, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

6. First, the recitation of "prevention of skin cells induced by UVB radiation" in the instant claims 19 and 25, direct the claims to methods of preventing a pathological condition. The specification fails to properly enable such methods. In the instant case, the burden of enabling for preventing wrinkle formation or age related skin manifestations requires appropriate screening testing, subsequent data compilation, and finally appropriate data analysis, to assess and properly enable one skill in the art whether skin cell immunosuppression are prevented in a patient. For example, the specification must provide adequate guidance whether immunosuppression can be prevented in a patient or in this case, a mammal, once the composition is administered to a subject susceptible to developing UVB induced immunosuppression.

7. Moreover, the specification must provide direct evidence associating the claimed prevention to the composition applied. The burden of showing preventative properties is greater than that of enabling a treatment, because one of ordinary skill in the art must not only show competent screening of those subjects susceptible to such conditions, but also show that the efficacy of a preventative method is directly caused by applying or administering the instantly claimed composition to the susceptible subjects. In the instant case, there is no teachings for screening methods identifying susceptible subjects nor is there any direct evidence of efficacy establishing a preventative property associated with the claimed composition.

8. Furthermore, the state of the prior art concerning methods of preventing immunosuppression of skin cells induced by UV-B is not well described, nor does it provide for any absolute prevention. Accordingly, undue experimentation is necessary

to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al US Patent 5,145,781 or Frazier US Patent 4,297,348.

11. The instant claims are directed to cosmetic or dermatological formulations comprising one or more flavonoids, optionally one or more cinnamic acid derivatives and optionally an antioxidant.

12. Applicant is informed that during patent examination, the pending claims are given the broadest reasonable interpretation consistent with the specification.

Accordingly, the recitation of "optionally" does not limit the instant formulations to the recited optional component.

13. Suzuki et al disclose α-glycosyl rutin which is a flavonoid encompassed by the instant claims. Suzuki discloses various uses of α-glycosyl rutin (col 8, lines 45-56; col 10, lines 4-30). Suzuki discloses cosmetic compositions comprising α-glycosyl rutin (see col 19-20). Therefore, Suzuki et al anticipates the limitations of the instant claim.

14. Frazier discloses topical compositions comprising naringin and naringenin (see example 7, claims 1-8). Accordingly, Frazier anticipates the limitations of the instant claims.

15. Claims 32-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Yoneyama et al US Patent 5,565,435.

16. Yoneyama et al disclose α-glycosyl quercetin derivatives in cosmetic compositions (see abstracts, col 14, lines 26-36). Yoneyama discloses α-glycosyl quercetin in combination with other flavonoids (see col 10, lines 65-68; col 11, lines 19-22, and lines 40-47). Accordingly, Yoneyama anticipates the instant claims.

17. Claim 30-33 is rejected under 35 U.S.C. 102(e) as being anticipated by Whittle US Patent 5,466,452.

Whittle discloses topical formulations for skin disorders comprising an extract of herbs (abstract; col 3, lines 63-65; examples 7-9). The constituents of each extract are disclosed in table 1. Accordingly, the extract ob Bei Yin Chen, for example, comprise flavonoids, caffeic acid, and the extract of Gan Cao comprise flavonoids in combination

with ferulic acid (see table 1, col 9-10; col 13, lines 35-39l; col 14, lines 50-52). Therefore, Whittle anticipates the limitations of the instant claim.

18. Claim 25-33 are rejected under 35 U.S.C. 102(e) as being anticipated by N'Guyen et al US Patent 5,431,912.

19. N'Guyen et al discloses cosmetic compositions comprising one or more flavonoids, caffeic acid derivatives and an antioxidizing agent such as beta carotene (see abstract; col 4, lines 15-21, col 8, lines 6-12; examples 1-5). The caffeic acid derivatives of N'Guyen anticipate the limitations of the instantly claimed cinnamic acid (col 2, lines 65-67; col 3, lines 1-12; col 7, lines 58-66; example 4). Finally, N'Guyen explicitly discloses topical application of his compositions for protecting the skin from oxidation (see col 5, lines 39-47). Therefore, N'Guyen anticipates the instant claim.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over N'Guyen et al US patent 5,587,171 in view of Middleton et al (Middleton) (Middleton and Chithan, *The Flavonoids, Advances in Research Since 1986*, 1994, Chapman & Hill, London, Ch. 15, pp 619-645), Harrrison's (*Harrison's Principles of Internal Medicine*, 1994, New York, McGraw-Hill, Inc., 13th edition, pp. 309-313).

The instant generic method claims are viewed according to their broadest reasonable interpretation, therefore, immunosuppression encompass any type of biological effects that cause attenuation of immune system.

N'Guyen et al discloses cosmetic compositions comprising one or more flavonoids including rutin, quercetin, and sugar derivatives thereof; caffeic acid derivatives and an antioxidizing agent such as beta carotene (see abstract; col 3, lines 23-65; col 4, lines 15-21, col 8, lines 6-12; examples 1-5). The caffeic acid derivatives of N'Guyen anticipate the limitations of the instantly claimed cinnamic acid (col 2, lines 65-67; col 3, lines 1-12; col 7, lines 58-66; example 4). N'Guyen also teaches the use of

said compositions as anti-sun creams and for protecting the lipids of the skin from oxidation (see col 5, lines 33-47). N'Guyen does not explicitly recite applications of his compositions on a subject for treating immunosuppression caused by UVB.

Middleton is merely used to show the plethora of information about the effects of flavonoids on immune system (pp 619-620). Accordingly, it is well within purview of an ordinary skill to modulate the activity of immune system by administering flavonoids of interest (Ch. 15, pp 619-645). For example, genistein have been shown to inhibit T-lymphocyte activity by inhibiting protein tyrosine kinase (see pp 625, 2nd col, 1st paragraph). Quercetin has been effective in regressing the spread of fibrosarcoma in vitro (see pp 627, 2nd col). Similarly, flavonal glycosides such as mauritanin and myricitrin have been shown to improve the delayed-type hypersensitivity among mice undergoing two-stage carcinogenesis (see top of pp 628). Moreover, topical quercetin has been effective in preventing and improving various immunosuppressive conditions associated with skin cancer (see pp 642, 3rd -8th paragraphs). Therefore, the general knowledge available in the art provides for the beneficial effects of topical flavonoids in improving immunosupresseive conditions regardless of their etiology.

Harisson's is used to show the general knowledge in the art about the etiology of solar radiation and systemic immune response caused by UV-B exposure (see pp 309 last paragraph). Accordingly, the immunesuppression caused by UV-B is caused by the induction of suppressor T cells throughout the body. Middleton and Harisson's collectively teach the general knowledge of an ordinary skill in the art of medicine and

immunology about the beneficial effects of flavonoids on immune system; and the etiology of immunosuprression cause by UV-B.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to apply N'Gyen's formulations topically to modulate immune suppressions caused by UV-B exposure, because as taught Harrison's, such immunosuprression is dependent on the activity of T-lymphocyte which as taught by Middleton, can be controlled by topical administration of a flavonoid of choice.

22. Moreover, the instant method claims 19 and 25 are not limited to any specific etiology associated with UV-B induced immunesuppression; rather, said claims are limited to the recitation of a single method steps, wherein the method comprise applying to the skin of a person an effective amount of one or more flavonoids, as recited in the body of the claim. Accordingly, the instant claims are prima facia obvious, because the ordinary skill in the art would have known of various beneficial effects of flavonoids on immune system when using N'Guyen's compositions topically.

N'Guyen patent teaches similar compositions as instantly claimed, except that it does not explicitly teach it the same pharmacological effects. In all other respects, the instant claims and the methods of N'Guyen are alike. The methods in which these compositions are employed are similar as they are directed to similar process steps. Thus, the method of use of N'Guyen's compositions are substantially identical in operation. Therefore, it would have been obvious to one of ordinary skill in the art understanding the etiology of UV-B induced skin conditions to apply N'Guyen's formulations for its immunologic effects because as taught by Middleton, the ordinary

skill in the art would have had a reasonable expectation of success for its beneficial immune effects.

Finally, Applicant is informed that the use of flavonoid in prophylactically treating or further treating UVB induced skin immunosuppression are well known in the art, as has been described in the cited prior art, and one skilled in the art would expect that compositions containing flavonoids, such as those thought by N'Guyen and Middleton would provide similar activity as the instantly claimed compositions, and accordingly, one skilled in the art would have known how to make and use such therapeutic composition. However, when the intended use is not as described by N'Guyen and Middleton, or it is directed to methods of preventing such conditions, Applicant has provided no guidance or working examples teaching one skilled in the art how to use such compositions in preventing immunosuppression of skin cells induced by UVB radiation. Therefore, based on the state of the prior art, lack of guidance and working examples, and the wide breadth of the claims 19-29; one skilled in the art could not use the entire scope of the claimed invention without undue experimentation.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 19-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 of U.S. Patent No. 5,952,373 ('373) and claims 1-5 of U.S. Patent 6,121,243 ('243). Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of both sets of claim overlaps in the manner that one renders the other obvious.

For example, claims 4 of '373 are directed to compositions comprising one or more flavonoid and other optional ingredients such as an antioxidant. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to make the similar compositions as instantly claimed.

Similarly, claims 1-5 of '243 are directed to methods of preventing or treating skin wrinkles against inflammation of skin caused by exposure to oxidation, which encompass sun and UVB exposure. Thus, the scope of the patented claims overlap with the scope of the pending claims and one of ordinary skill in the art would have been motivated to use the patented claims for the same reasons as instantly claimed invention.

25. Claim 19-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 009/656598 and 09/540007. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending

claims are directed to cosmetic compositions comprising one or more flavonoid, and other optional ingredients such as cinnamic acids and antioxidants. Therefore, the scopes of all pending claims overlap with each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, JD can be reached on 703-308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200

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May 7, 2002